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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,711	01/17/2002	Yunxiang Zhu	ZHUY 8216US	8638

1688 7590 09/30/2003

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EXAMINER

KHARE, DEVESH

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

10/051,711

Applicant(s)

ZHU, YUNXIANG

Examiner

Devesh Khare

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 16-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 4.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121:

- I. Claims 16-19, drawn to a glycoprotein, classified in class 530 and 536, subclass various.
- II. Claims 1-15, drawn to a process for coupling a mannopyranosyl oligosaccharide to a glycoprotein, classified in class 536, subclass various.
- III. Claims 20 and 21, drawn to a method of treating a lysosomal storage disease with the compounds of Group I, classified in class 514, subclass various.

The inventions are distinct, each from the other because of the following reasons:

Groups I to II are related as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for making the product as claimed can be practiced with another materially different process or (2) the product as claimed can be made in a materially different process of making that product (MPEP § 806.05(h)). In the instant case the claims are drawn to the

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process for coupling a mannopyranosyl oligosaccharide to a glycoprotein, indicating that the product can be prepared by a materially different method.

Groups I to III are related as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for making the product as claimed can be practiced with another materially different process or (2) the product as claimed can be made in a materially different process of making that product (MPEP § 806.05(h)). In the instant case the claims are drawn to a method of treating a lysosomal storage disease with the compounds of Group I, indicating that the product can be used by a materially different method.

Inventions II to III, are unrelated to one another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01).

Group II is drawn to a process for coupling a mannopyranosyl oligosaccharide to a glycoprotein, which is unrelated to method of treating a disease, of Group III.

Although the inventions are classified in the same class and sub-class, searching the three groups of inventions constitutes a burdensome search, as a thorough search comprises a search of foreign patents and non-patent literature as well as the appropriate U.S. patent classifications. Because these inventions are distinct for the

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reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper.

It is noted that the three independent and distinct inventions would indeed impose an undue burden upon the examiner in charge of this application.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143). If applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

(MPEP § 821.04)

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

A telephone call was made to Ned Randale on September 16, 2003 to request an oral election to the above restriction requirement. During telephone conversation with Ahaji Amoson September 17, 2003 a provisional election was made without traverse to prosecute the invention of Group II, claims 1-15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 16-21 are withdrawn from

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further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-15 are currently pending in this application.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- (A) Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the coupling of the phosphorylated mannopyranosyl oligosaccharide hydrazide derivative to the oxidized glycoprotein
- (B) Claim 4 is rejected under the second paragraph of 35 U.S.C. 112. Claim 4, depends on the method claim 3, directed to the method of claim 1, wherein the glycoprotein comprises a lysosomal enzyme is isolated from a natural source or produced in a recombinant expression system. The recitation in a dependent claim of "the source of an active agent" to be used in a method from which said claim depends, wherein "the source of said active agent" does not result in a patentably distinguishable methodological and manipulative difference in how

said active agent's source impacts the method from which it depends, renders the claim 4 in which it occurs and which depend therefrom indefinite for failing to distinctly articulate how such a recitation further limits the method from which said dependent claim 4, applicant regards as the invention.

(C) In claim 1, line 7, parenthetical description of a carbonyl group is superfluous and should be deleted.

(D) Claim 7 is rejected under the second paragraph of 35 U.S.C. 112. Claim 7, depends on the method claim 6, directed to the method of claim 1, wherein the M6P, phosphopentamannose is derived from *Hansenula holstii* O-phosphomannan. The recitation in a dependent claim of "the source of an active agent" to be used in a method from which said claim depends, wherein "the source of said active agent" does not result in a patentably distinguishable methodological and manipulative difference in how said active agent's source impacts the method from which it depends, renders the claim 4 in which it occurs and which depend therefrom indefinite for failing to distinctly articulate how such a recitation further limits the method from which said dependent claim 7, applicant regards as the invention.

(E) The phrase "can be substituted with oligosaccharides" in claim 10, line 2, is a relative phrase, which renders the claim indefinite. The phrase "can be substituted with oligosaccharides" does not particularly point out the substitution with oligosaccharide as their invention. The specification does not provide a standard for ascertaining the requisite degree of substitution with

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oligosaccharide, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(F) The phrase "highly phosphorylated mannopyranosyl oligosaccharide" in claim 1, is a relative phrase, which renders the claim indefinite. The phrase "highly phosphorylated mannopyranosyl oligosaccharide" does not particularly point out the sites at which the mannopyranosyl oligosaccharide is phosphorylated. The specification does not provide a standard for ascertaining the requisite degree of phosphorylation of the mannopyranosyl oligosaccharide, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(G) Claims 1 and 12 are vague and indefinite as it is unclear whether the phrase "chemical compound(s)" is intended to be included as a chemical compound containing carbonyl-reactive groups such as a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound or any other compound.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolvanen et al. (J.B.C., 261,20, 9546-9551, 1986) in view of Monsigny et al. (U.S. Patent 6,251,858).

The claims 1-15 are directed to a method for coupling a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein, which is defined as: derivatizing the phosphorylated mannopyranosyl oligosaccharide with a chemical compound containing a carbonyl-reactive group; oxidizing the glycoprotein having at least one glycan to generate at least one aldehyde group on the glycoprotein; and reacting the oxidized glycoprotein with the derivatized phosphorylated mannopyranosyl oligosaccharide.

Additional claim limitations set forth in dependent claims include the oxidizing agent periodate or galactose oxidase, glycoprotein is a lysosomal enzyme, phosphorylated mannopyranosyl oligosaccharide contains at least one mannose 6-phosphate of the general formula 6-P-M_n-R and includes biantennary or triantennary mannopyranosyl oligosaccharide containing bis-M6P or tri-M6P, phosphorylated mannopyranosyl oligosaccharide can be replaced with oligosaccharides containing the terminal hexoses such as galactose, mannose, GlcNAc and fucose, the chemical compound containing carbonyl-reactive groups comprises a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound and a cyanoborohydride reagent to reduce the hydrazone bond.

Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates (see abstract). Tolvanen et al. disclose that a hydrazine derivative of any available carbohydrate can be introduced into an oxidized cell surface glycoconjugates (see page 9546, 2nd col., 4th para.). The glycosylhydrazines of the blood group A active heptasaccharide (containing gal, GlcNAc and fucose) were coupled to periodate-oxidized cells in supplemental material col.1-2 (see coupling of glycosylhydrazines to erythrocytes and K562 cells). Tolvanen et al. also disclose the use of mannosylhydrazine in the coupling reaction (see page 9547, fig. 11 and 2nd. para). While Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates, Tolvanen et al. differ from applicant's process in that Tolvanen et al. do not suggest the coupling of a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein such as lysosomal enzyme.

Monsigny et al. teach the coupling of derivatives of oligosaccharides by covalent means to a protein (see abstract). Monsigny et al. discloses the biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate (see col. 16, g, lines 43-54). Monsigny et al. disclose the oligosaccharides containing the terminal hexoses such as galactose, mannose, GlcNAc and fucose (see col. 15, lines 30-50). Monsigny et al. also disclose the use of sodium cyanoborohydride to reduce the imine formed between the reducing sugar and the amine (col.3, lines 28-33).

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It is noted that Monsigny et al. do not suggest a method of coupling an oxidized glycoprotein with the derivatized phosphorylated mannopyranosyl oligosaccharide.

Therefore, one of ordinary skill in the art would have found the applicants claimed method of coupling a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein, to have been obvious at the time the invention was made having the above cited references before him. Since Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates and Monsigny et al. discloses the coupling of biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate to a protein, one skilled in the art would have a reasonable expectation for success in combining both references to accomplish a method for coupling a oligosaccharide derivative by reacting with the aldehyde groups generated in the oxidized carbohydrates on glycoproteins to form covalent bond conjugates. The motivation for doing so is provided by Tolvanen et al., which suggests that the glycosylhydrazines can be covalently coupled into the oxidized cell surface glycoproteins without affecting their biological activities (see page 9546, col. 2, 3rd. para.).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (703)605-

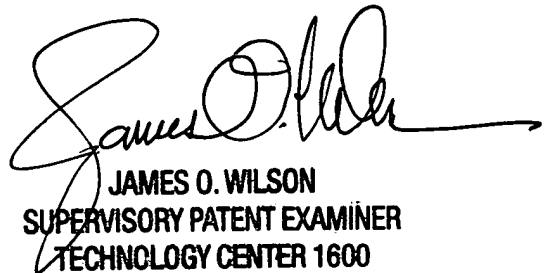
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1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
September 26,2003



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600